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L6 ANSWER 1 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2000:218282 BIOSIS
DN PREV200000218282
TI Sendai virus blocks alpha interferon signaling to signal transducers and activators of transcription.
AU Komatsu, Takayuki (1); Takeuchi, Kenji; Yokoo, Junko; Tanaka, Yukie; Gotoh, Bin
CS (1) Department of Microbiology, Fukui Medical University School of Medicine, Shimoaizuki 23-3, Matsuoka-cho, Yoshida-gun, Fukui, 910-1193 Japan
SO Journal of Virology, (**March**, **2000**) Vol. 74, No. 5, pp. 2477-2480.
ISSN: 0022-538X.
DT Article
LA English
SL English
AB We demonstrate here that Sendai virus (SeV) blocks alpha interferon (IFN-alpha) signaling to signal transducers and activators of transcription (STATs) in HeLa cells. IFN-alpha-stimulated tyrosine phosphorylation of STATs and subsequent formation of the IFN-stimulated gene factor 3 transcription complex were **inhibited** in SeV-infected cells, resulting in inefficient induction of IFN-stimulated gene products. None of the components of the signaling pathway-type I IFN receptor subunits Jak1, Tyk2, Stat1, Stat2, and **p48**-was degraded. Moreover, tyrosine phosphorylation of Jak1 in response to IFN-alpha was unaffected at the early phase of infection, suggesting that **oligomerization** of the receptor subunits proceeded normally. In contrast to Jak1, IFN-alpha-stimulated tyrosine phosphorylation of Tyk2 was partially **inhibited**. Therefore, this partial **inhibition** of activation of Tyk2 probably contributes to the subsequent failure in the activation of STATs.

L6 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2000:454069 BIOSIS
DN PREV200000454069
TI Interaction of retinoic acid and interferon in renal cancer cell lines.
AU Nanus, David M. (1); Geng, Yiping; Shen, Ruoqian; Lai, Hui-Kang; Pfeffer, Susan R.; Pfeffer, Lawrence M.
CS (1) New York Presbyterian Hospital, Weill Medical College of Cornell University, 520 E. 70th Street, ST-341, New York, NY, 10021 USA
SO Journal of Interferon and Cytokine Research, (**September**, **2000**) Vol. 20, No. 9, pp. 787-794. print.
ISSN: 1079-9907.
DT Article
LA English
SL English
AB Retinoic acid (RA) can potentiate the antitumor effect of interferons (IFN) in a variety of tumor types, including renal cell carcinoma (RCC). The mechanisms by which RA and IFN increase the antitumor effects in RCC are unknown. We used growth assays and mobility shift assays to examine the effects of combining 13-cis-retinoic acid (CRA) and IFN-alpha (plus IFN-gamma) on proliferation and on the expression of the IFN-specific transcription factor IFN-stimulated gene factor 3 (ISGF3) in RCC cell lines. Combining CRA and IFN-alpha resulted in a significant increase in growth **inhibition** in four cell lines compared with IFN-alpha or CRA alone. Binding of nuclear extracts from RCC cells to an IFN-stimulated response element (ISRE) **oligonucleotide** probe following

incubation with IFN-alpha was not increased by CRA but was significantly increased by pretreatment by IFN-gamma in a time-dependent fashion. Proliferation assays showed that sequential addition of IFN-gamma and IFN-alpha significantly increased growth **inhibition**. IFN-alpha but not IFN-gamma or CRA increased the cellular levels Stat2 and **p48** but not Stat1. IFN-gamma pretreatment enhanced the upregulation of **p48** levels by IFN-alpha. Combining RA and IFN results in additive growth **inhibition** on RCC cell lines. This increase in growth **inhibition** is not mediated by increased ISGF3 expression.

L6 ANSWER 3 OF 16 SCISEARCH COPYRIGHT 2002 ISI (R) DUPLICATE 3
AN 2001:63113 SCISEARCH
GA The Genuine Article (R) Number: 388VN
TI Human cytomegalovirus **inhibition** of interferon signal transduction
AU Miller D M (Reprint); Cebulla C M; Sedmak D D
CS Ohio State Univ, Coll Med, Dept Pathol, Columbus, OH 43210 USA
CYA USA
SO JOURNAL OF MICROBIOLOGY, (**DEC 2000**) Vol. 38, No. 4, pp. 203-208. Publisher: MICROBIOLOGY SOC KOREA, KOREA SCIENCE & TECHNOLOGY CENTER 803, 635-4 YEOGSAM-DONG, KANGNAM-KU, SEOUL 135-703, SOUTH KOREA. ISSN: 1225-8873.
DT General Review; Journal
LA English
REC Reference Count: 61
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Cytomegalovirus (CMV), a beta-herpesvirus with worldwide distribution, exhibits host persistence, a distinguishing characteristic of all herpesviruses. This persistence is dependent upon restricted gene expression in infected cells as well as the ability of productively infected cells to escape from normal cell-mediated anti-viral immunosurveillance, Type I(IFN-alpha/beta) and type II (IFN-gamma) interferons are major components of the innate defense system against viral infection. They are potent inducers of MHC class I and II antigens and of antigen processing proteins. Additionally, IFNs mediate direct antiviral effects through induction of effector molecules that block viral infection and replication, such as 2', 5-**oligoadenylate** synthetase (2, 5-OAS). IFNs function through activation of well-defined signal transduction pathways that involve phosphorylation of constituent proteins and ultimate formation of active transcription factors. Recent studies have shown that a number of diverse viruses, including CMV, EBV, HPV, mumps and Ebola, are capable of **inhibiting** IFN-mediated signal transduction through a variety of mechanisms. As an example, CMV infection **inhibits** the ability of infected cells to transcribe HLA class I and II antigens as well as the antiviral effector molecules 2, 5-OAS and MxA I. EMSA studies have shown that IFN-alpha and IFN-gamma are unable to induce complete signal transduction in the presence of CMV infection, phenomena that are associated with specific decreases in JAK1 and **p48**. Viral **inhibition** of IFN signal transduction represents a new mechanistic paradigm for increased viral survival, a paradigm predicting widespread consequences in the case of signal transduction factors common to multiple cytokine pathways.

L6 ANSWER 4 OF 16 CA COPYRIGHT 2002 ACS
AN 132:31744 CA
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Ltd., UK
SO PCT Int. Appl., 745 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9964627	A2	19991216	WO 1999-GB1780	19990604 <--

PI WO 9964627 A2 19991216 WO 1999-GB1780 19990604 <--

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1998-12099 A 19980606
GB 1998-13291 A 19980620
GB 1998-13611 A 19980624
GB 1998-13835 A 19980627
GB 1998-14110 A 19980701
GB 1998-14580 A 19980707
GB 1998-15438 A 19980716
GB 1998-15574 A 19980718
GB 1998-15576 A 19980718
GB 1998-16085 A 19980724
GB 1998-16086 A 19980724
GB 1998-16921 A 19980805
GB 1998-17097 A 19980807
GB 1998-17200 A 19980808
GB 1998-17632 A 19980814
GB 1998-17943 A 19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L6 ANSWER 5 OF 16 CA COPYRIGHT 2002 ACS
AN 132:31743 CA

TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Limited, UK
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9964626	A2	19991216	WO 1999-GB1779	19990604 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9941586	A1	19991230	AU 1999-41586	19990604 <--
	AU 9941587	A1	19991230	AU 1999-41587	19990604 <--
	GB 2339200	A1	20000119	GB 1999-12914	19990604 <--
	GB 2339200	B2	20010912		
	EP 1084273	A1	20010321	EP 1999-925207	19990604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI	GB 1998-12098	A	19980606
	GB 1998-28289	A	19981223
	GB 1998-16086	A	19980724
	GB 1998-16921	A	19980805
	GB 1998-17097	A	19980807
	GB 1998-17200	A	19980808
	GB 1998-17632	A	19980814
	GB 1998-17943	A	19980819
	WO 1999-GB1779	W	19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

DUPLICATE 4

L6 ANSWER 6 OF 16 MEDLINE
AN 1999248195 MEDLINE
DN 99248195 PubMed ID: 10229853
TI Human cytomegalovirus **inhibits** IFN-alpha-stimulated antiviral and immunoregulatory responses by blocking multiple levels of IFN-alpha signal transduction.
AU Miller D M; Zhang Y; Rahill B M; Waldman W J; Sedmak D D

CS Department of Pathology, Ohio State University, Columbus, OH 43210, USA.
NC RO1 AI38452-01A1 (NIAID)
SO JOURNAL OF IMMUNOLOGY, **(1999 May 15)** 162 (10) 6107-13.
Journal code: IFB; 2985117R. ISSN: 0022-1767.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199906
ED Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990614
AB The type I IFNs represent a primordial, tightly regulated defense system against acute viral infection. IFN-alpha confers resistance to viral infection by activating a conserved signal transduction pathway that up-regulates direct antiviral effectors and induces immunomodulatory activities. Given the critical role of IFN-alpha in anti-human cytomegalovirus (HCMV) immunity and the profound ability of HCMV to escape the host immune response, we hypothesized that HCMV blocks IFN-alpha-stimulated responses by disrupting multiple levels of the IFN-alpha signal transduction pathway. We demonstrate that HCMV **inhibits** IFN-alpha-stimulated MHC class I, IFN regulatory factor-1, MxA and 2',5-**oligoadenylate** synthetase gene expression, transcription factor activation, and signaling in infected fibroblasts and endothelial cells by decreasing the expression of Janus kinase 1 and **p48**, two essential components of the IFN-alpha signal transduction pathway. This investigation is the first to report **inhibition** of type I IFN signaling by a herpesvirus. We propose that this novel immune escape mechanism is a major means by which HCMV is capable of escaping host immunity and establishing persistence.

L6 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 2000:84452 BIOSIS
DN PREV200000084452
TI Suppression of interferon response gene expression in cells persistently infected with mumps virus, and restoration from its suppression by treatment with ribavirin.
AU Fujii, Nobuhiro (1); Yokosawa, Noriko; Shirakawa, Sachiko
CS (1) Department of Microbiology, School of Medicine, Sapporo Medical University, South 1, West 17, Chuou-Ku, Sapporo, Hokkaido, 060 Japan
SO Virus Research, (**Dec. 15, 1999**) Vol. 65, No. 2, pp. 175-185.
ISSN: 0168-1702.
DT Article
LA English
SL English
AB Persistent infections with mumps virus were established in human B-lymphoid cell line Akata and in the human chronic myelogenous leukaemia cell line K562. Even after IFN treatment a drastic decrease in STAT-1alpha (signal transducers and activators of transcription-1alpha), STAT-2 and **p48** (ISGF-3gamma: IFN-stimulated gene factor-3gamma), which are closely correlated with the IFN-signaling pathway, was found in these persistently infected cells (Akata-MP1 and K-MTP). Therefore, the IFN-signaling pathway is thought to be defective in these persistently infected cells. In other words, most of the IFN-inducible genes in these cells persistently infected with mumps virus may not be able to respond to IFN treatment. Indeed, poor induction of 2',5'-**oligoadenylate** synthetase (2-5AS), dsRNA activated protein kinase (PKR), and MxA protein mRNAs were demonstrated in these cell lines after IFN treatment. Expression of MHC class-I antigen was also significantly reduced in the persistently infected cell lines as compared with that of uninfected control cells. HLA antigen was augmented by IFN-alpha in Akata and K562

cells, but not in persistently infected cells. Furthermore, suppression of IFN-induced 2-5AS induction and MHC class-I expression was restored by treatment of persistently infected cells with ribavirin through **inhibition** of virus replication. The result of restoration was also confirmed by IFN-induced STAT-1 induction in persistently infected cells treated with ribavirin.

L6 ANSWER 8 OF 16 CA COPYRIGHT 2002 ACS
AN 129:94275 CA
TI IFN-.gamma. priming up-regulates IFN-stimulated gene factor 3 (ISGF3) components, augmenting responsiveness of IFN-resistant melanoma cells to type I IFNs
AU Wong, Lee, H.; Hatzinisiriou, Irene; Devenish, Rodney J.; Ralph, Stephen J.
CS Dep. Biochemistry Molecular Biology, Monash Univ., Clayton, Australia
SO J. Immunol. (**1998**), 160(11), 5475-5484
CODEN: JOIMA3; ISSN: 0022-1767
PB American Association of Immunologists
DT Journal
LA English
AB IFN-stimulated gene factor 3 (ISGF3) mediates transcriptional activation of IFN-sensitive genes (ISGs). The component subunits of ISGF2, STAT1.alpha..beta., STAT2, and **p48**-ISGF3.gamma., are tyrosine phosphorylated before their assembly into a complex. Subsequently, the ISGF3 complex is translocated to the nucleus. The authors have recently established that the responsiveness of human melanoma cell lines to type I IFNs correlates directly with their intracellular levels of ISGF3 components, particularly STAT1. Here, the authors show that pretreating IFN-resistant melanoma cell lines with IFN-.gamma. (IFN-.gamma. priming) before stimulation with type I IFN also results in increased levels of ISGF3 components and enhanced DNA-binding activation of ISGF3. In addn., IFN-.gamma. priming of IFN-resistant melanoma cell lines increased expression of type I IFN-induced ISG products, including ISG54, 2'-5'-**oligoadenylate** synthase, HLA class I, B7-1, and ICAM-1 antigens. Furthermore, IFN-.gamma. priming enhanced the antiviral effect of IFN-.beta. on the IFN-resistant melanoma cell line, MM96. These results support a role for IFN-.gamma. priming in up-regulating ISGF3, thereby augmenting the responsiveness of IFN-resistant melanoma cell lines to type I IFN and providing a mol. basis and justification for using sequential IFN therapy, as proposed by others, to enhance the use of IFNs in the treatment of melanoma.

L6 ANSWER 9 OF 16 MEDLINE DUPLICATE 6
AN 1998418938 MEDLINE
DN 98418938 PubMed ID: 9748142
TI Interferon-alpha-induced activation of signal transducer and activator of transcription proteins in malignant melanoma.
AU Carson W E
CS Department of Surgery, Ohio State University, Columbus 43210, USA.
NC CA68326 (NCI)
SO CLINICAL CANCER RESEARCH, **(1998 Sep)** 4 (9) 2219-28.
Journal code: C2H; 9502500. ISSN: 1078-0432.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199811
ED Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981120
AB IFN-alpha2b has been used to treat patients with malignant melanoma who are at high risk for recurrence after surgical resection. However, its

exact mechanism of action is unknown. I hypothesized that IFN-alpha exerts a direct effect on the melanoma cell via the activation of signal transducer and activator of transcription (STAT) proteins. Cell lysates from melanoma cell lines and patient tumor samples stimulated with IFN-alpha were incubated with radiolabeled **oligonucleotides** representing the high affinity sis-inducible element of c-fos and the IFN stimulated response element and then analyzed for STAT activation using the electrophoretic mobility shift assay. Melanoma cell lines showed no evidence for constitutive STAT activation in the absence of cytokine stimulation but exhibited rapid activation of STAT1 and STAT2 once treated with IFN-alpha. A distinct dose-response curve was noted with maximal STAT activation occurring at approximately 10(5) units/ml IFN-alpha. Genistein, a protein tyrosine kinase **inhibitor**, completely suppressed IFN-alpha-induced STAT activation. Malignant melanoma tumors obtained from 17 patients exhibited dose-dependent activation of STAT1 and STAT2 in response to treatment with IFN-alpha. Pretreatment of patient melanoma tumor cells with IFN-gamma resulted in a 4 log-fold decrease in the IFN-alpha concentration required for STAT activation and promoted the increased expression of STAT1, STAT2, and **p48**. In summary, IFN-alpha consistently activated STAT1 and STAT2 proteins in melanoma cell lines and in melanoma tumors obtained directly from patients. This signaling pathway was dramatically sensitized to IFN-alpha by pretreatment of melanoma cells with low concentrations of IFN-gamma. These results provide molecular evidence to support the hypothesis that the clinical response to IFN-alpha may be mediated, in part, by a direct effect on the melanoma cell. These results also suggest a potential role for IFN-gamma in the treatment of malignant melanoma.

L6 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7

AN 1997:306310 BIOSIS

DN PREV199799614113

TI Retinoic acid induces signal transducer and activator of transcription (STAT) 1, STAT2, and **p48** expression in myeloid leukemia cells and enhances their responsiveness to interferons.

AU Matikainen, Sampsa (1); Ronni, Tapani; Lehtonen, Anne; Sareneva, Timo; Melen, Krister; Nordling, Stig; Levy, David E.; Julkunen, Ilkka

CS (1) Natl. Public Health Inst., Mannerheimitie 166, FIN-00300 Helsinki Finland

SO Cell Growth & Differentiation, (1997) Vol. 8, No. 6, pp. 687-698. ISSN: 1044-9523.

DT Article

LA English

AB IFNs are antiproliferative cytokines that have growth-**inhibitory** effects on various normal and malignant cells. Therefore, they have been used in the treatment of certain forms of cancer, such as chronic myelogenous leukemia and hairy cell leukemia. However, there is little evidence that IFNs would be effective in the treatment of acute myelogenous leukemia, and molecular mechanisms underlying IFN unresponsiveness have not been clarified. Here we have studied the activation and induction of IFN-specific transcription factors signal transducer and activator of transcription (STAT) 1, STAT2, and **p48** in all-trans-retinoic acid (ATRA)-differentiated myeloid leukemia cells using promyelocytic NB4, myeloblastic HL-60, and monoblastic U937 cells as model systems. These cells respond to ATRA by growth **inhibition** and differentiation. We show that in undifferentiated NB4 cells, 2',5'-**oligoadenylate** synthetase and MxB gene expression is not activated by IFN-alpha, possibly due to a relative lack of signaling molecules, especially **p48** protein. However, during ATRA-induced differentiation, steady-state STAT1, STAT2, and especially **p48** mRNA and corresponding protein levels were elevated both in NB4 and U937 cells, apparently correlating to an enhanced responsiveness of these cells

to IFNs. ATRA treatment of NB4 cells sensitized them to IFN action as seen by increased IFN-gamma activation site DNA-binding activity or by efficient formation of IFN-alpha-specific ISGF3 complex and subsequent **oligoadenylate** synthetase and MxB gene expression. Lack of **p48** expression could be one of the mechanisms of promyelocytic leukemia cell escape from growth-**inhibitory** effects of IFN-alpha.

L6 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 8
AN 1996:375905 BIOSIS
DN PREV199699098261
TI A serine-kinase associated with the **p127**-l(2)gl tumour suppressor of Drosophila may regulate the binding of **p127** to nonmuscle myosin II heavy chain and the attachment of **p127** to the plasma membrane.
AU Kalmes, Andreas; Merdes, Gunter; Neumann, Beate; Strand, Dennis (1); Mechler, Bernard M.
CS (1) Dep. Dev. Genet., Deutsches Krebsforchungszentrum, Im Neuenheimer Feld 280, D-69120 Heidelberg Germany
SO Journal of Cell Science, (1996) Vol. 109, No. 6, pp. 1359-1368. ISSN: 0021-9533.
DT Article
LA English
AB The **p127** tumour suppressor protein encoded by the lethal(2)giant larvae, (l(2)gl), gene of Drosophila melanogaster is a component of a cytoskeletal network distributed in both the cytoplasm and on the inner face of the plasma membrane. The **p127** protein forms high molecular mass complexes consisting mainly of homo-**oligomerized** **p127** molecules and at least ten additional proteins. One of these proteins has been recently identified as nonmuscle myosin type II heavy chain. To determine the functional interactions between **p127** and other proteins present in the **p127** complexes, we analyzed **p127** for posttranslational modifications and found that **p127** can be phosphorylated at serine residues. In this report we describe the characteristics of a serine kinase which is associated with **p127**, as judged by its recovery in **p127** complexes purified by either gel filtration or immuno-affinity chromatography. This kinase phosphorylates **p127** in vitro and its activation by supplementing ATP results in the release of **p127** from the plasma membrane. Moreover, similar activation of the kinase present in immuno-purified **p127** complexes dissociates nonmuscle myosin II from **p127** without affecting the homo-**oligomerization** of **p127**. This dissociation can be **inhibited** by staurosporine and a 26mer peptide covering amino acid positions 651 to 676 of **p127** and containing five serine residues which are evolutionarily conserved from Drosophila to humans. These results indicate that a serine-kinase tightly associated with **p127** regulates **p127** binding with components of the cytoskeleton present in both the cytoplasm and on the plasma membrane.

L6 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 9
AN 1994:531674 BIOSIS
DN PREV199497544674
TI Transcriptional induction of genes by IFN-beta in mouse cells is regulated by a transcription factor similar to human ISGF-3.
AU Kalvakolanu, Dhananjaya V. (1); Mannino, Sara B.; Thornton, Angela; Ozato, Keiko; Borden, Ernest C.
CS (1) Univ. Md. Cancer Cent., Univ. Md. Sch. Med., 22 S. Greene St., Baltimore, MD 21201 USA
SO Antiviral Research, (1994) Vol. 25, No. 2, pp. 91-103.

ISSN: 0166-3542.
DT Article
LA English
AB Previous studies of IFN-stimulated transcription factors in murine cells have identified a variety of trans-acting factors that bind to the IFN-stimulated response element (ISRE) whose role in gene expression remain unclear. The present investigation was undertaken to delineate the signal transduction pathway as well as to identify the transcription factors regulated by murine IFN-beta in L929 cells. Tyrosine kinase **inhibitor**, Genistein, abrogated gene induction and activation of transcription factors by IFN-beta. As early as 5 min after IFN-beta treatment, a transcription factor was activated in the cytoplasm which subsequently migrated into the nucleus. Anti-phosphotyrosine antibodies detected a specific transcription factor induced by mIFN-beta. Antibodies raised against human ISGF-3 subunit proteins **p48**, p84, p91 and p113 recognized this factor in the cytoplasm as well as in the nucleus of IFN-beta-treated L929 cells. An antibody raised against an **oligopeptide** of human p113 (residues 435-450) recognized the ISGF-3 complexes both in human and murine cells. However. a different antibody against the C-terminus of human p113 (residues 671-806) did not recognize the ISGF-3 like complex in mouse cells, indicating differences in the primary sequence of these proteins.

L6 ANSWER 13 OF 16 MEDLINE
AN 93252924 MEDLINE
DN 93252924 PubMed ID: 8387518
TI The DNA helicase activities of Rad3 protein of Saccharomyces cerevisiae and helicase II of Escherichia coli are differentially **inhibited** by covalent and noncovalent DNA modifications.
AU Naegeli H; Modrich P; Friedberg E C
CS Department of Pathology, University of Texas Southwestern Medical Center, Dallas 75235-9072.
NC CA12428 (NCI)
GM23719 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1993 May 15)** 268 (14) 10386-92.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930618
Last Updated on STN: 19970203
Entered Medline: 19930608
AB Rad3 protein of Saccharomyces cerevisiae is a DNA-dependent ATPase that acts as a DNA helicase on partially duplex substrates. Rad3 **protein** is required for **damage-specific** incision of **DNA** during the nucleotide excision repair (NER) pathway in yeast. Helicase II of Escherichia coli is also a DNA helicase, but it is involved in postincision events in NER. Previous investigations have demonstrated that the DNA helicase activities of Rad3 protein and helicase II are both **inhibited** by DNA damage. In the present study we have compared the response of yeast Rad3 protein and E. coli helicase II to a broad spectrum of DNA modifications. The Rad3 helicase activity is considerably more sensitive to ultraviolet radiation damage and cisplatin adducts in DNA than to drugs that interact noncovalently with duplex DNA. Conversely, E. coli helicase II is highly sensitive to noncovalent DNA modifications but less sensitive than Rad3 protein to ultraviolet radiation damage or cisplatin adducts. We also show that Rad3 protein and helicase II differ in their ability to form stable protein-DNA complexes at sites of DNA damage. Hence, DNA helicases that catalyze

distinct steps in NER respond differently to chemical and conformational states of the DNA substrate. The observation that Rad3 protein is particularly sensitive to covalent but not noncovalent alterations in DNA structure is consistent with the hypothesis that this enzyme may have adopted a highly specialized role in damage-specific recognition during NER.

L6 ANSWER 14 OF 16 CA COPYRIGHT 2002 ACS
AN 119:40435 CA
TI Cisplatin-DNA damage recognition proteins in human tumor extracts
AU Bissett, D.; McLaughlin, K.; Kelland, L. R.; Brown, R.
CS CRC Dep. Med. Oncol., Glasgow, UK
SO Br. J. Cancer (**1993**), 67(4), 742-8
CODEN: BJCAAI; ISSN: 0007-0920
DT Journal
LA English
AB Enhanced repair of DNA adducts may be a cause of cis-diamminedichloroplatinum(II) resistance in solid malignancies. Binding of specific damage recognition proteins to the sites of DNA damage may be involved in the initial steps of DNA repair, or alternatively may block access of repair proteins to damaged DNA. Proteins which bind specifically to CDDP-modified DNA were identified in cell exts. from human ovarian carcinoma cell lines by two assays, the gel mobility shift assay and the southwestern blot. In the first assay, proteins complexed with CDDP-modified **oligonucleotide** and produced two retarded bands, B1 and B2. The B2 complex was partially purified from an ovarian cell ext. by anion exchange FPLC, and was shown to bind to DNA damaged by CDDP but not by transDDP or UV irradn. Using the southwestern blot, proteins of 97, 48, and 25 kD were identified; each of these bound to CDDP-modified but not undamaged **oligonucleotide**. The partially purified B2 protein fraction contained both the 97 and the 25 kD damage recognition proteins. A human ovarian carcinoma cell line selected in vitro for CDDP-resistance (OV1P/DDP), which is 5-fold more resistant to CDDP than the parental line (OV1P), showed an increase in binding of the 97 and 48 kD damage recognition proteins compared with the parental line. Twelve ovarian cell lines differed by up to 3-fold in their expression of these proteins, but there was no correlation between the amt. of damage recognition protein in a cell ext. and the cellular sensitivity to CDDP. Damage recognition proteins were also demonstrated in exts. prepd. from biopsies of human ovarian, cervical, and testicular malignancies, but there was no apparent difference in the binding activity in exts. from tumors of different CDDP-sensitivity. The functional role of these damage recognition proteins remains to be established.

L6 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 10
AN 1992:95047 BIOSIS
DN BA93:51597
TI THE DNA HELICASE AND ADENOSINE TRIPHOSPHATASE ACTIVITIES OF YEAST RAD3 PROTEIN ARE **INHIBITED** BY DNA DAMAGE A POTENTIAL MECHANISM FOR DAMAGE-SPECIFIC RECOGNITION.
AU NAEGELI H; BARDWELL L; FRIEDBERG E C
CS LAB. MOL. PATHOL., DEP. PATHOL., UNIV. TEXAS SOUTHWESTERN MED. CENTER DALLAS, DALLAS, TEXAS 75235.
SO J BIOL CHEM, (1992) 267 (1), 392-398.
CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB Purified Rad3 protein from the yeast Saccharomyces cerevisiae is a single-stranded DNA-dependent ATP-ase and also acts as a DNA helicase on partially duplex DNA. In this study we show that the DNA helicase activity is **inhibited** when a partially duplex circular DNA substrate is

exposed to ultraviolet (UV) radiation. **Inhibition** of DNA helicase activity is sensitive to the particular strand of the duplex reigon which carrier the damage. **Inhibition** is retained if the single-stranded circle is irradiated prior to annealing to an unirradiated **oligonucleotide**, but not if a UV-irradiated **oligonucleotide** is annealed to unirradiated circular single-stranded DNA. UV irradiation of single-stranded DNA or deoxyribonucleotide homopolymers also **inhibits** the ability of these polynucleotides to support the hydrolysis of ATP by Rad3 protein. UV radiation damage apparently blocks translocation of Rad3 protein and results in the formation of stable Rad3 protein-UV-irradiated DNA complexes. As a consequence, Rad3 protein remains sequestered on DNA, presumably at sites of base damage. The sensitivity of Rad3 protein to the presence of DNA damage on the strand along which it translocates provides a potential mechanism for damage recognition during nucleotide excision repair and may explain the absolute requirement for Rad3 **protein** for **damage-specific** incision of **DNA** in yeast.

L6 ANSWER 16 OF 16 CA COPYRIGHT 2002 ACS
AN 116:79400 CA
TI Interleukin 1(beta) protease
IN Black, Roy A.; Sleath, Paul R.; Kronheim, Shirley R.
PA Immunex Corp., USA
SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9115577	A1	19911017	WO 1991-US2339	19910404 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	AU 9177759	A1	19911030	AU 1991-77759	19910404 <--
	US 5416013	A	19950516	US 1994-203716	19940228 <--
PRAI	US 1990-505298	A	19900404		
	US 1991-656759	A	19910213		
	WO 1991-US2339	A	19910404		
	US 1991-750644	B1	19910830		

OS MARPAT 116:79400
AB The cDNA for interleukin 1.beta. protease of humans is cloned and expressed in CHO cells. The protease can be used in pharmaceuticals for treatment of e.g. arthritis and autoimmune diseases (no data). The substrate specificity of the protease was detd. with synthetic peptides, and **inhibitors** Z-A-Asp-B (Z = N-terminal protecting group; A = 0-4 amino acids; B = electroneg. leaving group) were prepd. and tested.

=> d his

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L2 339 S L1 AND INHIBIT?
L3 652673 S L2 AND ANTISENSE OR OLIGO?
L4 50 S L2 AND (ANTISENSE OR OLIGO?)
L5 42 S L4 AND PY=<2000
L6 16 DUP REMOVE L5 (26 DUPLICATES REMOVED)

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